Remarks

Claims 1-30 were pending in the subject application. The Office Action indicates that claims 25-30 have been withdrawn as being drawn to non-elected subject matter.

By this Amendment, the applicants have amended claims 1, 2, 9, 10, 17 and 18, have cancelled claims 25-30 and have added new claims 31-33. Support for the amendments to claims 1, 9 and 17 can be found at, for example, page 14, lines 31-32 of the specification. Support for the amendments to claims 2, 10 and 18 can be found at, for example, page 6, lines 9-12 of the subject specification. Support for new claim 31 can be found at, for example, page 31, lines 15-24 of the specification and support for new claims 32 and 33 can be found at, for example, page 31, line 27 through page 32, line 5 of the subject specification. No new matter has been added by these amendments. Accordingly, claims 1-24 and 31-33 are before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

The applicants wish to thank Examiners Singh and Marx for the courtesy extended to the undersigned during the Examiner Interview conducted on May 6, 2008. This response and the amendments set forth herein are submitted in accordance with the substance of that interview and constitute a summary thereof.

Claims 2, 10 and 18 have been rejected under 35 USC §112, second paragraph. The applicants respectfully traverse this rejection to the extent that it might be applied to the claims now presented for examination.

Please note that claims 2, 10, and 18 have been amended herein for clarification to replace the phrase "wherein the source of said milk protein hydrolysate is selected from ..." with "wherein said milk protein hydrolysate is a hydrolysate of a milk protein selected from ...." Support for the amendments to claims 2, 10 and 18 can be found at, for example, page 6, lines 9-12 of the subject specification.

Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph.

Claims 1-24 have been rejected under 35 USC §103(a) as being unpatentable over Gray *et al.* in view of Kawai *et al.*, Davis *et al.* and Siegenthaler, taken with Fritsche *et al.* and Ohashi *et al.* The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the applicants' unique composition or its use.

As discussed in detail below, a skilled artisan would have had no reason to combine the teachings of the cited references to arrive at the current invention.

The applicants claim a composition, and its use, wherein the composition has a specified amount (0.9 to 3 g per 100 ml) of milk protein hydrolysate, as well as a specified amount (2.5 to 4.5 g per 100 ml) of protein derived from fermented milk. As discussed in detail below, and in the attached Expert Declaration, the protein from fermented milk contains substantial quantities of whole proteins. The subject composition also contains other specified ingredients, including palatinose in an amount of 4 to 15 grams per 100 ml.

The composition claimed by the current applicants differ from the composition disclosed by the primary Gray *et al.* reference in several important aspects. First, the claimed composition has less total protein than the composition that is disclosed by Gray *et al.* The total protein content in the current applicants' composition is 3.4 to 7.5 g/100 mL of the composition. This is significantly less than the preferable amount of protein in the product disclosed by Gray *et al.* at column 6, lines 13-15, which is 94 grams/liter (*i.e.*, 9.4 g/100 mL).

Next, the claimed composition has much less protein hydrolysate than the Gray *et al.* composition. Gray *et al.* disclose at column 4, lines 5-8 that "the protein source includes approximately 80% to 85% of protein hydrolysate." Thus, the preferable amount of protein hydrolysate in the formulation of Gray *et al.* is 7.52 to 7.99 g/100 mL, which greatly exceeds the amount of milk protein hydrolysate in the nutritional composition of the present invention.

Finally, while the claimed composition has an important and significant whole protein component, Gray *et al.* repeatedly emphasize that their composition does not have any whole protein.

For example, at column 2, lines 56-60 and at columns 8 and 9, Contemplative Example No. 1, Gray *et al.* emphasize the advantages of not using whole proteins.

In the personal Examiner interview mentioned above, the Examiners expressed the opinion that there might be very little whole protein in fermented milk product, and that, therefore, the Examiners were discounting the significance of the difference in whole protein content between the claimed invention and the composition of Gray *et al.* Submitted herewith, as part of an Expert Declaration under 37 CFR §1.132, are experimental results that establish that fermented milk products, as recited in the current applicants' claims, do contain substantial amounts of undegraded (whole) proteins. This is exactly the type of protein that Gray *et al.* wished to avoid.

As described in the Declaration, chromatographic analysis of milk before fermentation in comparison to analysis of samples of milk following fermentation finds little protein degradation resulting from fermentation. Test 1 compares the protein present in milk before fermentation to three samples of fermented milk. The fermented milk was found to retain between 88-95% of proteins following the fermentation process. Thus, the fermented milk samples do not exhibit substantial breakdown of the whole proteins in milk, including casein, β-lactoglobulin, and α-lactalbumin.

The Examiner has also indicated that the milk hydrolysate may not be very different from fermented milk. Specifically, the outstanding Office Action indicates that the total of the two sources of protein in the applicants' composition, namely the whey protein hydrolysate and fermented milk, should be compared to the 7.52 g per mL as described by Gray *et al.* The applicants respectfully disagree.

The accompanying Expert Declaration provides an analysis of the whole protein content of whey protein isolate. Figure 2 includes an analysis of a whey protein hydrolysate in lanes 5 and 8. The results confirm significant whole protein degradation, as evidenced by a lack of any visible protein banding for the whey protein hydrolysate as compared to the fermented milk. Test 3 substantiates this finding using gel filtration chromatography. Figure 3 displays the results and illustrates the extent of whole protein degradation. The chromatographic peak is noted at 1 kDa

which corroborates the degradation and lack of whole proteins, such as the higher molecular weight casein, β-lactoglobulin, and α-lactalbumin of milk.

The applicants reiterate that the disclosure of Gray *et al.* emphasizes that whole proteins should be avoided. The 7.52 g per mL of Gray *et al.* is composed of a degraded protein hydrolysate. Gray *et al.* explicitly extoll the virtues of avoiding whole protein. In direct contrast to the teachings of Gray *et al.*, the applicants' composition comprises whole protein from fermented milk at 2.5-4.5 g per mL. This represents a great difference in whole protein content between the Gray *et al.* composition and the applicants' invention.

In addition to failing to appreciate the extent and significance of the differences in protein content between the claimed composition and the composition of Gray *et al.*, the outstanding Office Action incorrectly combines the teachings of the secondary reference with the teachings of Gray *et al.* As discussed below, the skilled artisan would have had no motivation, or expectation of success, to combine the disparate teachings of the various cited references to arrive at the current applicants' advantageous composition.

First, with regard to the Ohashi *et al.* reference, which is relied upon in the outstanding Office Action to address the deficiencies of the Gray *et al.* reference with respect to the protein content of the composition, there is no apparent reason why the skilled artisan would even consider combining the teachings of these two references. Specifically, Ohashi *et al.* do not disclose or suggest the use of their elemental diet for patients under high levels of invasive stress, nor does Gray *et al.* describe the use of the enteral formulation for patients with hepatic disorder. Accordingly, the skilled artisan would have had no motivation to combine these teachings in the first place.

Furthermore, even if these references were somehow combined, one would not arrive at the current invention. Ohashi *et al.* describe a <u>low protein</u> diet of amino acids, carbohydrates, fats, vitamins, and minerals. Gray *et al.* explicitly disclose at column 2, lines 47-50 that "an advantage of the present invention is to provide a composition having <u>a high protein content</u>," (emphasis added) and at column 3, lines 57-59 Gray *et al.* state that "due to increased metabolic activity, such patients require high protein intake to reduce negative nitrogen balance and support wound repair."

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

The teachings of Ohashi *et al.* are opposite to the purpose of the enteral formulation of Gray *et al.*, and thus, a skilled artisan would have had no motivation to combine the two teachings to arrive at the current invention.

The Office Action indicates that it would have been obvious to a person of ordinary skill in the art to modify the composition of Gray *et al.*, in view of Siegenthaler, such that it includes a protein from fermented milk, such as quark. The applicants respectfully disagree.

Gray *et al.* disclose at column 2, lines 56-60 that "nutrient malabsorption is reduced by the absence of whole proteins" and at column 8, lines 58-60 that "[m]any of the patients receiving the whole protein diet were unable to receive the recommended calorie and protein intakes ... because of intolerance and diarrhea and conflicts with the need to not overhydrate."

The fermented milk of Siegenthaler contains significant amounts of whole proteins; therefore, one skilled in art would not have been motivated to combine the teachings of Siegenthaler with that of Gray *et al.* Thus, the applicants respectfully submit that one of ordinary skill in the art would have had no reason to combine fermented milk products into the enteral formulation of Gray *et al.*

The Office Action further suggests that it would have been obvious to a person of ordinary skill in the art to modify the composition of Gray *et al.*, such that it includes a milk protein hydrolysate that is obtained by enzymatic hydrolysis of a whey protein isolate (WPI).

Davis *et al.* primarily aim at suppressing angiotensin-converting enzyme (ACE), and providing a composition effective therefor. Nowhere in the disclosure of Davis *et al.* is there a suggestion of applying enzymatically hydrolyzed whey proteins to patients under high level of invasive stress. As noted in the Office Action, MPEP 2144.06, stipulates that "[i]t is prima facie

obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose (emphasis added)." However, the purpose of the composition of Davis *et al.* containing enzymatically hydrolyzed whey proteins, is completely different from the purpose of the enteral formulation of Gray *et al.*, the former being for suppressing ACE activity and the later being for providing nutritional support to a trauma, burn or post-surgery patient. The applicants respectfully submit that it would not have been obvious to a skilled artisan to modify the composition of Gray *et al.* such that it includes a protein hydrolysate obtained by enzymatic hydrolysis of a WPI, nor would there have been a reasonable expectation of success.

The Office Action also indicates that it would have been obvious to a person of ordinary skill in the art to modify the composition of Gray *et al.* such that it includes a non-calorigenic carbohydrate such as palatinose, because Kawai *et al.* discloses a non-calorigenic substitute for carbohydrate source.

The applicants would like to bring the Examiner's attention to column 2, lines 51-55 of Gray *et al.* which discloses that "an advantage of the present invention is to provide a composition that has reduced water and carbohydrate content, reducing the risk of diarrhea due to carbohydrate intolerance, hyperglycemia..." (emphasis added).

As per MPEP 2143.01, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Further, if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

A person with ordinary skill in the art would not have had motivation to use palatinose as discussed by Kawai *et al.* in the reduced carbohydrate composition of Gray *et al.* Please note that the claims have been amended herein to recite that the composition of the subject invention has 4 to 15 grams per 100 ml of palatinose.

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969).

For the reasons explained above, one of ordinary skill in the art would not combine Gray *et al.* with the cited secondary references to arrive at the current invention. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §103(a) is respectfully requested.

Claims 1-24 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 37 and 38 of copending Application No. 10/487,237. The applicants would like to defer substantive response to this rejection until allowable subject matter has been established in the current application, or until the copending application has matured into a patent.

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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Attachments: Expert Declaration of Ms. Hisae Kume under 37 CFR §1.132
Experimental Data